infants and children) to penicillin and cephalosporins mandates the empiric use of vancomycin, pending definitive identification and sensitivity testing of the bacterial isolate. Physicians caring for hospitalized patients, in addition to carefully selecting antibiotics for the empiric therapy of critically ill patients, must limit the use of broad-spectrum antibiotics that perpetuate multiple drug resistance and predispose these patients to superinfections.

The increase of antimicrobial resistance demands the attention of all physicians. Antibiotics must be used judiciously: the overzealous use of antibiotics in the past has resulted in our compromised ability to manage bacterial infections today. It is only through the thoughtful prescription of antibiotics that the balance between antibiotic use and drug resistance can be regained. Our obligation extends beyond our individual patients to the entire community of patients for whom we are responsible.

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Advances in the Treatment of Respiratory Failure in Newborns

ENORMOUS STRIDES in the treatment of respiratory failure have significantly reduced neonatal mortality and morbidity. Recent advances in technology that target specific respiratory disease processes have further improved the outlook for newborns with respiratory failure.

Hyaline membrane disease (HMD), a major cause of mortality and morbidity in premature infants, is caused by a surfactant deficiency. Extensive animal studies and clinical trials have shown that surfactant replacement is effective in both preventing HMD ("prophylactic" treatment) and treating established HMD ("rescue" treatment). Two forms of replacement surfactant are available for clinical use: Survanta, a modified bovine surfactant, and Exosurf, a totally synthetic surfactant. Infasurf, another modified calf lung surfactant extract, will likely be approved by the FDA soon. In addition to its role in the treatment of infants with HMD, surfactant may be useful for the treatment of other diseases characterized by surfactant deficiency or inactivation, such as meconium aspiration syndrome.

Improved ventilator technology has played an important role in managing neonatal respiratory failure. Intermittent mandatory ventilation (IMV) was the standard mode of therapy for treatment of HMD for more than 30 years. With IMV, a fixed number of breaths is delivered at defined intervals, and the patient has no control over the timing of the breaths. Today, patient-triggered ventilation and high frequency ventilation (HFV) have largely replaced IMV. Synchronized intermittent mandatory ventilation (SIMV) and assist/control ventilation (ACV) allow the patient to adjust the timing of breaths by "triggering" the ventilator. Both SIMV and ACV deliver more uniform breaths than does IMV, and they cause less ventilator-induced variation in arterial blood pressure. SIMV gives a fixed number of breaths each minute, but the breaths are synchronized with the patient's respiratory effort. With ACV, each patient effort is assisted by the ventilator. Clinical trials of both SIMV and ACV suggest that infants ventilated with these patient-triggered modes are extubated sooner than infants ventilated with IMV.

High frequency ventilation (HFV) is principally used in managing critically ill neonates with severe restrictive lung disease, such as respiratory distress syndrome, meconium aspiration, and pulmonary hypoplasia. Unlike conventional ventilators that mimic normal tidal breathing, HFV delivers extremely small breaths at rates as high as 900 breaths per minute. Although these "breaths" are often as small as or smaller than dead space volume, they are able to achieve effective gas exchange primarily by causing gas mixing between the upper airway and the alveoli. The three main forms of high frequency ventilation are high frequency oscillatory ventilation (HFOV), high frequency jet ventilation (HFJV), and high frequency flow interruption (HFFI). HFOV uses an oscillating diaphragm that delivers a sinusoidal pressure wave to the patient, usually at rates between 600 and 900 breaths per minute. HFJV injects small, high velocity, "jets" of gas into the airway, usually at 420 breaths per minute, and operates in conjunction with a conventional ventilator, using a triple-lumen endotracheal tube adapter that allows both ventilators to be connected to the patient simultaneously. HFFI "interrupts" the flow of gas to the upper airway, generating high frequency breaths that have some of the characteristics of both HFOV and HFJV breaths. Studies have yielded conflicting results about possible increased neurological morbidities associated with these techniques.

When ventilatory methods fail in term and near-term infants, extracorporeal membrane oxygenation (ECMO) is the next line of therapy. ECMO is a form of prolonged cardiopulmonary bypass, allowing support of infants with severe pulmonary failure. There are two types: venous to arterial and venous to venous. The use of ECMO at designated centers—most commonly for newborns with severe meconium aspiration, pulmonary hypertension, or diaphragmatic hernia—has dramatically reduced the mortality of these disorders. The average responder requires less than a week of ECMO therapy and then is returned to ventilatory support. One major complication from ECMO is intracranial hemorrhage secondary to anticoagulation therapy. A second major complication is the loss of the carotid artery when venous-to-arterial ECMO is used and

the carotid artery is not reconstructed. The long-term neurodevelopmental sequelae of ECMO are unknown.

Research continues to evaluate treatments for infants with severe respiratory distress. Two investigational pharmacologic agents show great promise but are not in use outside of research protocols. Nitric oxide (NO), a potent pulmonary vasodilator, reverses pulmonary hypertension, a major component of many neonatal lung diseases. It acts by decreasing pulmonary vascular resistance and improving oxygenation. Another agent, perfluorocarbon, is a dense liquid in which oxygen and carbon dioxide are soluble. When used to fill the lungs in a process called liquid ventilation, it provides gas exchange and decreases atelectasis, improves pulmonary blood flow, and decreases lung inflammation.

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Helicobacter pylori Infection: Pediatric Aspects

HELICOBACTER PYLORI is a major cause of peptic ulcer disease in children. Although discovered in the early 1900s, *H pylori's* role in human gastrointestinal disease was appreciated only upon its successful culture by Marshall and Warren in 1983. Numerous studies in adults and children have established a strong association between *H pylori* colonization and both antral gastritis and peptic ulcer disease. Most children and adults infected with *H pylori*, however, have no apparent symptoms, and few will develop peptic ulcer disease.

H pylori is a spiral, gram-negative, urease-producing organism that infests the area between the gastric epithelium and the overlying layer of mucosa. Initial infection with *H pylori* usually occurs in childhood via fecal-oral transmission. Familial clustering of cases suggests either person-to-person or common-source acquisition. Vertical transmission from mother to newborn infant appears to be rare; breastfeeding may provide some degree of protection from *H pylori* infection during infancy. The prevalence of colonization increases with age in developed countries, with approximately 10% of children infected by age 10. In non-industrialized countries and in lower socioeconomic groups, up to 50% of children are positive for *H pylori* by age 10.

H pylori colonization produces a chronic infection with variable clinical consequences. Virtually all infected individuals have histologic evidence of antral gastritis, but the majority are asymptomatic. A relatively small percentage of infected children will develop peptic ulcer disease, but of those with peptic ulcer disease, the incidence of *H pylori* supports a causal connection. In a review of 18 pediatric studies by Macarthur et al, the median prevalence of *H pylori* infection was 92% in children with duodenal ulcers and 25% in those with gastric ulcer disease. The factors that influence the ultimate clinical course of *H pylori* remain largely unknown. One reason that some individuals develop peptic ulcer disease while most remain asymptomatic may be variability in *H pylori* strains. Individual strains containing the cytotoxic-associated gene A (*cagA*) appear to cause more severe gastritis and an increased incidence of peptic ulcer disease. An individual's immunologic responses may also affect the course of *H pylori* infection.

The importance of *H pylori*–associated gastritis, in the absence of peptic ulcer disease, remains controversial. At best, there is a weak and inconsistent relationship between *H pylori* and "classic" recurrent abdominal pain of childhood (vague peri-umbilical pain without associated diarrhea, weight loss, or nocturnal awakening). *H pylori* has been strongly associated with the development of gastric adenocarcinoma and gastric MALT lymphoma. Since the incidence of gastric cancer is three to six times higher in *H pylori*–infected individuals, the World Health Association's International Agency for Research on Cancer has classified *H pylori* as a "Group 1" (definite) carcinogen.

Diagnosis of *H pylori* infection can be accomplished by both non-invasive and endoscopic techniques. In general, non-invasive tests are useful as initial screens, and endoscopy is reserved for confirming peptic ulcer disease or when upper gastrointestinal bleeding occurs or treatment fails. Non-invasive tests consist of serology by immunoassays (e.g., ELISA) and urea breath tests. Both have a high sensitivity and specificity. Urea breath tests are based on the measurement of breath ^{14}C or ^{13}C-labeled CO_2 produced when urease-producing *H pylori* organisms in the stomach split labeled urea. During endoscopy, *H pylori* can be identified by histologic evaluation of gastric mucosal biopsies and by the rapid urease test, in which a biopsy sample is placed in a gel containing urea and a pH indicator. If the tissue contains *H pylori* organisms, urease will split the urea, liberating ammonia and raising the pH, causing a change in the gel color from yellow to pink. Cultures of gastric biopsies are not routinely performed because of their difficulty and expense.

Treatment is currently recommended for all patients with *H pylori*–associated peptic ulcer disease. Without treatment, infection appears to be lifelong, since spontaneous remission is rare. Eradication of *H pylori* dramatically decreases ulcer recurrence and may also decrease the recurrence of complications, such as hemorrhage. Treatment is complicated by the relative resistance of *H*